Poster II-3

Computer Simulation of Breast Cancer Data Suggests Explanation for Paradoxical Mammography Results

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Several breast cancer databases for patients who were not treated with adjuvant chemotherapy showed a peculiar double peaked relapse hazard pattern. The relapse peaks included a sharp peak at 1.5 years, a nadir at 4 years and a broad peak at 5-6 years with a long tail extending to 15 or more years. Using computer simulation of a simple growth model, we proposed that the second peak was the natural history of the disease while the first peak represented events that would have happened later but were stimulated to occur earlier somehow by events near the time of surgery.

From the timing of relapses, computer simulation suggested that surgery could precipitate angiogenesis in dormant distant disease for premenopausal node- positive patients.

With this information, we examined the mammography controversy, since it is plausible that such a process might explain the paradoxical results for women age 40-49. For those women, at three years after screening starts, there is a statistically significant surge in mortality among screened compared to unscreened women (1). According to our explanation, angiogenesis of dormant tumors produces relapses within one year of surgery and, since the survival duration after relapse is approximately 2 years, the entire sequence would manifest as mortality at 3 years (2).

There are several biological mechanisms that were proposed to explain how surgery could speed up breast cancer. Angiogenesis inhibitors are produced by tumors as clearly demonstrated in animal models and suggested in clinical cancer such as lung and melanoma. Therefore, removing tumors would remove the source of the inhibitors, which could produce a wave of angiogenesis of dormant disease. Another mechanism is the appearance of growth factors in response to surgical wounding. Among these growth factors are tumor growth factors.

This does not mean that women age 40-49 should not be screened. It does mean that we should learn how to control this stimulated angiogenesis. We have suggested administering antiangiogenic drugs at the time of surgery and also timing surgery to the luteal phase of the menstrual cycle since during that time, endogenous pro-angiogenesis factors are at a minimum. Federal grant support: none.

References

1. Cox B. Variation in the effectiveness of breast screening by year of follow-up. J Natl Cancer Inst Monogr 22:69-72, 1997
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